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1: J Clin Invest 1995 Jun;95(6):2806-12

Increased abundance of the receptor-type protein-tyrosine phosphatase LAR accounts for the elevated insulin receptor dephosphorylating activity in adipose tissue of obese human subjects.

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Protein-tyrosine phosphatases (PTPases) have an essential role in the regulation of the steady-state phosphorylation of the insulin receptor and other proteins in the insulin signalling pathway. To examine whether increased PTPase activity is associated with adipose tissue insulin resistance in human obesi we measured PTPase enzyme activity towards the insulin receptor in homogenates of subcutaneous adipose tissue from a series of six lean and six nondiabetic, obese (body mass index > 30) subjects. The obese subjects had a mean 1.74-fold increase in PTPase activity ($P < 0.0001$) with a striking positive correlation by linear regression analysis between PTPase activi and body mass index among all of the samples ($R = 0.918$; $P < 0.0001$). The abundance of three candidate insulin receptor PTPases in adipose tissue was also estimated by immunoblot analysis. The most prominent increase was a 2.03-fold rise in tl transmembrane PTPase LAR ($P < 0.001$). Of the three PTPase examined, only immunodepletion of LAR protein from the homogenates with neutralizing antibodies resulted in normalization of the PTPase activity towards the insulin recepto demonstrating that the increase in LAR was responsible for the enhanced PTPase activity in the adipose tissue from obese subjects. These studies suggest that increased PTPase activity towards the insulin receptor is a pathogenetic factor in the insul resistance of adipose tissue in human obesity and provide